THE COUNCIL FOR TOBACCO RESEARCH–U.S.A., INC.

cc: RCH
JHK
FWN

July 24, 1973

MEMORANDUM FOR FILE

SUBJECT: Grant 786R2.
H. Hugh Fudenberg, M.D.
"Collagen Antibodies in Relation to the Etiology of Emphysema."
Site Visit July 10, 1973.

Dr. Fudenberg had a pile of manuscripts, reports and reprints assembled and we went too rapidly down the stack.

First, he made it clear that he wanted a smoke delivery machine. They could use it for in vitro and in vivo experiments. They had some in vivo studies completed. Smoke was bubbled through media and added to fibroblast cultures. It caused the cells to round up but not necessarily die. They, I believe, lost their collagen synthetic capacity. Collagen synthesis in vitro was followed by H^3 or C^{14} proline incorporation. S^{35} was used for hyaluronic acid. Acetaldehyde in amounts possibly comparable to smoke delivery amounts produced the same effects on fibroblasts. He was vague about quantitation or I was vague on uptake but 1/8 cig. per 1 ml media or equivalent to 1/8 was the figure I recall.

Chemically he has overcome the lack of solubility difficulty by different digests, pepsin digests, cyanogen bromide disassociation, SS fractures and obtained a^1, a^2 and b chains. Some amino acid sequencing has been done. He is comparing collagen from emphysematous lungs with that of normal lungs and fetal lungs and dermal collagen, fetal and adult. Collagen in different tissues differs, probably a greater organ specificity than species specificity. Seems to be different collagenasis in different tissues.

Fudenberg is keeping away from mice because of the histo-compatability antigens which complicate the immunology probably more than HLA antigens.

Fine structure. He showed me many fine scan, freeze, et al., and freeze fracture ems. of the collagen of lung and tail. A manuscript has been submitted to J. Ultrastructure giving a somewhat new idea of collagen structure. Photographs of composite chains, fractures, cross-linkages (propyl nitrile) treated. Em. photo of emphysematous lungs seems to show consistent changes.

Phagocytic activity. Type 1 cells were shown in em. with large vacuoles containing one or more rbc, sometimes also in vacuoles and partially resolved. Mitochondria of these cells showed mitochondrial increase in number and size. Some studies were being done using cortisol and insulin.

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The studies on patients have now reached 150, about half of the proposed number. This will be completed during the year. Fudenberg aware of the limitations of genetic analyses by IA and developing a method of computer analyses of enzymatic inhibitions.

A Dr. Warner from Australia who has done much work on mouse antigens is going to be in the laboratory until January. Dr. Wells would like to stay one more year. Wells is working on the CEA specificity and has apparently found a specific antigen for lung cancer.

Fudenberg is planning to do more on cell immunity and is preparing fluorescence and rhubidium label materials - antigens - for such studies.

Fudenberg gave me two manuscripts and will shortly send more preprints. He may contact us about Wells. I'll be interested in seeing the work on tumor specific lung cancer antigens.

W.U.G.

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